

Chemoselective Deprotection/Oxidation of Protected Alcohols with Magtrieve™

Sung-Tae Park and Kwang-Youn Ko*

Department of Chemistry, Ajou University, Suwon 442-749, Korea

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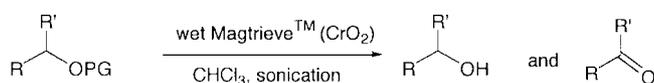
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Selective protection and deprotection of functional groups is important in organic synthesis.¹ Hydroxyl groups are often protected as their ethers or acetals/ketals, which can be deprotected under a wide variety of conditions. Such ethers include 1-ethoxyethyl (EE) ether, 1-methyl-1-methoxyethyl (MIP) ether, tetrahydropyranyl (THP) ether, methoxymethyl (MOM) ether, 2-methoxyethoxymethyl (MEM) ether and *tert*-butyldimethylsilyl (TBDMS) ether, for example.

Magtrieve™ (Dupont Product), a magnetically retrievable oxidant (CrO₂), was first used for the oxidation of alcohols in high yields.² We have already shown that this reagent can also be used as an oxidant for other functional groups such as Hantzsch 1,4-dihydropyridines,³ hydrazone,⁴ and thiols.⁵ Interestingly, we have found that wet Magtrieve™ can deprotect acetals derived from carbonyl compounds or further oxidize aldehydes to carboxylic acids under neutral condition.⁶ As an extension of this study, we investigated the possibility of employing Magtrieve™ for the deprotection/oxidation of hydroxyl protecting groups including EE, MIP, THP, MOM, MEM, and TBDMS ethers (Scheme 1).⁷

Deblocking was performed by subjecting a mixture of ether and a small amount of water (5 equiv) in purified CHCl₃ to sonication in the presence of Magtrieve™ under N₂ atmosphere and the results are presented in Table 1. First, deprotection of EE ether of benzyl alcohol was studied under several conditions. Reaction at room temperature without sonication or at refluxing temperature for 2 days gave a mixture of alcohol and aldehyde (entries 1a-b). Refluxing at toluene provided aldehyde in high yield through the further oxidation of the deprotected alcohol (entry 1c). Sonication in CHCl₃ gave deprotected alcohol contaminated with a small amount of aldehyde within 12 h (entry 1d). Prolonged reaction gave aldehyde ultimately in high yield (entry 1e). Because deprotection/oxidation under sonication occurred in a milder condition, the remaining deprotections were performed under this condition.⁸ Similarly, EE ethers of allylic alcohols were cleanly converted to aldehydes under sonication (entries 2-3). In contrast, EE ethers of aliphatic alcohols were converted into their corresponding alcohols without further oxidation (entries 4-7).

PG = EE, MIP, THP, MOM, MEM, TBDMS



Scheme 1

Compared to EE ethers derived from alcohols, EE ether from phenol underwent slower deprotection (entry 8).

Table 1. Deprotection/oxidation of protected alcohols^a with Magtrieve™

Entry	Substrates	Products ^b		Time
		Alcohols	Aldehydes or Ketones	
1a	PhCH ₂ OEE	50% ^c	20%	2 days ^d
1b		30%	55% ^c	2 days ^e
1c		0%	95%	1 day ^f
1d		75%	18%	12 h
1e		0%	94%	1 day
2	PhCH=CHCH ₂ OEE	0%	92%	1 day
3	Me ₂ C=CHCH ₂ OEE	0%	93%	2 days
4	<i>n</i> -C ₈ H ₁₇ OEE	84%	5%	6 h
5	Me(CH ₂) ₃ CH(Et)CH ₂ OEE	93%	0%	6 h
6	ClCH ₂ CH(OEE)CH ₂ Cl	91%	0%	8 h
7	<i>n</i> -C ₆ H ₁₃ CH(Me)OEE	91%	3%	7 h
8	<i>m</i> -MeC ₆ H ₄ OEE	60% ^c		3 days
9a	PhCH ₂ OMIP	90%	5%	1 h
9b		0%	93%	2 day
10a	PhCH=CHCH ₂ OMIP	90%	5%	1 h
10b		0%	94%	1 days
11	<i>n</i> -C ₈ H ₁₇ OMIP	92%	0%	1 h
12	Me(CH ₂) ₃ CH(Et)CH ₂ OMIP	92%	0%	3 h
13	ClCH ₂ CH(OMIP)CH ₂ Cl	91%	0%	2 h
14	<i>n</i> -C ₆ H ₁₃ CH(Me)OMIP	92%	0%	1 h
15	PhCH ₂ OTHP	5%	45% ^c	2 days
16	PhCH=CHCH ₂ OTHP	10%	20% ^c	2 days
17	<i>n</i> -C ₈ H ₁₇ OTHP	No reaction		2 days
18	<i>m</i> -MeC ₆ H ₄ OTHP	No reaction		3 days
19	PhCH ₂ OMOM	5%	20% ^c	2 days
20	<i>n</i> -C ₈ H ₁₇ OMOM	23% ^c	0%	3 days
21	<i>n</i> -C ₆ H ₁₃ CH(Me)OMOM	44% ^c	0%	3 days
22	PhCH=CHCH ₂ OMEM	0%	10% ^c	2 days
23	<i>n</i> -C ₈ H ₁₇ OMEM	32% ^c	3%	2 days
24	<i>n</i> -C ₆ H ₁₃ CH(Me)OMEM	41% ^c	0%	2 days
25	PhCH ₂ OTBDMS	No reaction		3 days
26	PhCH=CHCH ₂ OTBDMS	No reaction		3 days

^aDeprotection was performed by treating a solution of ethers (1.0 mmol) and water (90 mg, 5 equiv) in purified CHCl₃ (10 mL) with Magtrieve™ (1.51 g) and subjecting the mixture to sonication without additional heating under N₂ atmosphere during the specified time. ^bIsolated yields for the major products. Yields of less than 5% were calculated from a ¹H-NMR spectrum. ^cThe rest is the starting compound. ^dWithout sonication. ^eReflux in CHCl₃. ^fReflux in toluene.

MIP ethers of allylic or benzyl alcohols were easily deblocked to alcohols within 1 h and these alcohols were further oxidized to aldehydes (entries 9-10). MIP ethers of aliphatic alcohols were more rapidly deprotected to alcohols than EE ethers (entries 11-14), as expected.^{1a}

However, ethers such as THP (entries 15-17), MOM (entries 19-21), MEM (entries 22-24) and TBDMS ethers (entries 25-26) were reluctant to undergo the deprotection. Also, phenolic THP ether was inert to the reaction condition (entry 18). The inertness of these protective groups was exemplified by the chemoselective removal of EE ether in the presence of THP, MOM, or MEM ether. Thus, treatment of a mixture of EE and THP ethers of 1-octanol with MagtrieveTM for 6 h resulted in the clean deprotection of EE ether, with THP ether intact. Similarly, EE ether of 1-octanol was selectively deprotected in the presence of MOM or MEM ethers upon treatment with wet MagtrieveTM for 6 h.

In summary, the present study shows that wet MagtrieveTM

can be used for the chemoselective deprotection/oxidation of EE and MIP ethers in the presence of THP, MOM, MEM or TBDMS ether.

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